DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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Via Federal Express

WARNING LETTER

Lawrence P. Bogle, M.D., Chair
Institutional Review Board
Mission Bay Memorial Hospital
3030 Bunker Hill Street
San Diego, California 92109

Dear Dr. Bogle:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB). The inspection took place during the period of January 25 through 28, 2000, and was conducted by Mr. Allen F. Hall, an investigator from FDA's Los Angeles District Office. The purpose of the inspection was to determine whether your procedures complied with Title 21, Code of Federal Regulations (21 CFR), Part 50-Protection of Human Subjects, Part 56-Institutional Review Boards, and Part 812 – Investigational Device Exemptions. These regulations apply to clinical studies of products regulated by the FDA.

Our review of the inspection report submitted by the district office revealed serious violations from pertinent regulations. You received a form FDA-483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations noted and discussed with you. The deviations noted include the following:

Failure to maintain adequate records (21 CFR 56.115).
IRB records are incomplete in that they did not contain copies of all research proposals; all correspondence between the IRB and investigators; documentation of the qualifications, representative capacity and institutional affiliation of all IRB members; and all meeting minutes. Moreover, meeting minutes do not provide sufficient detail to show attendance at the minutes; actions taken by the IRB; and the vote on these actions, including the number of members voting for, against, and abstaining.

Failure to conduct continuing review of on-going research at least yearly [21 CFR 56.108(a)(1, 2)].
A progress report for an ongoing study was dated 12/29/98 and noted that the previous progress report was 1/5/97. The 12/98 report was reviewed at an IRB meeting on 1/5/99.

Failure to follow written procedures (21 CFR 56.108).
Meeting minutes were not signed by the IRB chair as required by the IRB's written procedures.

The deviations listed above are not intended to be an all-inclusive list of deficiencies. The IRB is responsible for adhering to each requirement of the law and relevant regulations.

Moreover, review of the Institutional Review Committee Charter included with the inspection report revealed the following:

- There are no written procedures for making significant risk/non-significant risk decisions regarding investigational studies of medical devices, as described in 21 CFR 812.66.

- Duties with regard to continuing review read "obtaining a periodic update." Procedures need to reflect the fact that continuing review must occur at least yearly and include a process for determining which projects require review more often [21 CFR 56.115(a)(6)].

- Under CRITERIA FOR APPROVAL OF STUDIES, item 1 reads "The study is being conducted with appropriate FDA approval and review." Significant risk device studies do require approval of an Investigational Device Exemption (IDE) by FDA. Non-significant risk device studies, however, require only review and approval by the reviewing IRB, as described in the *Abbreviated requirements* found in 21 CFR 812.2(b).

- Item 3 under DUTIES includes temporary and emergency approval of investigational studies. Regulations allow for expedited approval of minimal risk studies and minor changes to approved studies. These are covered in 21 CFR 56.110. This is different from what is implied by the term "temporary approval." Moreover, 21 CFR 56.104(c) allows for emergency, one-time use of an investigational product, as long as such use is reported to the IRB within 5 working days of use. No prior permission is required.

- Under Item 6 of CRITERIA FOR APPROVAL OF STUDIES, the essential elements of informed consent documents are included. Those required are listed in 21 CFR 50.25. Your listing is missing a statement that the study involves research as well as a listing of the persons study subjects can contact. These contacts are to include someone to whom adverse effects or concerns are to be reported; who can answer general questions about research studies; and with whom to discuss complaints or concerns about the particular study. The last of these contacts should be someone not directly connected with the study in question.

Mr. Hall has informed us that he received a phone call on March 2, 2000, advising him that the IRB is closing down. Please confirm in writing, within 15 working days, that the IRB is no longer functioning. Also, please include a listing of all investigational studies reviewed by the IRB over the last 5 years. This listing needs to include the present

status of each study, i.e., when it was closed or terminated or the name of the IRB to which review has been transferred, as well as the date of official transfer.

Please send the information requested to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Jean Toth-Allen, Ph.D.

If a future decision should result in reconstitution of this IRB, all deviations noted above must be corrected before investigational studies can be reviewed. A copy of a revised IRB Charter (Standard Operating Procedures), as well as a commitment to abide by all pertinent regulations, would need to be submitted to this office for review.

A copy of this letter has been sent to FDA's Los Angeles District Office, 19900 MacArthur, Suite 300, Irvine, California 92715. We request that a copy of your response also be sent to that office.

If you have any questions, feel free to contact Jean Toth-Allen at (301) 594-4723, ext. 141.

Sincerely yours,

Marvin A. Bonner, RPh

for Lillian J. Gill
Director
Office of Compliance
Center for Devices and Radiological Health

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